

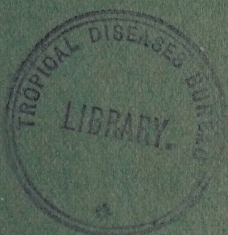
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ORIENTAL SORE.



By S. T. Darling, M.D., ANCON HOSPITAL,
CANAL ZONE.

Reprinted from THE JOURNAL OF CUTANEOUS DISEASES
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ORIENTAL SORE.*

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ORIENTAL sore (dermal leishmaniosis) is an infective granuloma of the skin, usually ulcerative in character, appearing most often on an exposed part of the body and occurring endemically in certain tropical and sub-tropical localities. It is caused by an intracellular protozoön, *Leishmania tropica*, and appears to be transmitted by dipterous insects, either in the act of biting or by mechanically infecting the broken skin.

The discovery of this disease in several places in the New World—Brazil and Guiana, and by the writer in the Canal Zone, naturally suggests the likelihood of its being encountered in Central America, Mexico and some of the Southern States. This paper is presented before the Society for the purpose of calling attention to the disease on that account.

HISTORICAL SKETCH.

Although a diagnostic criterion for this affection was not established until 1903 by Wright, the disease has been well known and has been described by travelers from the East for many years. The first serious account of the disease was that of Russell.¹ Other accounts were published by travelers and temporary residents of Aleppo, such as those of Dr. Holland, Alibert, Disant, Guilhou and Willemin.² The last made a study of the disease during a sojourn in Aleppo in 1852. From his description we learn that the disease was known in certain towns and villages in the valleys of the Tigris and Euphrates—Aintab, Diarbekir (38° N.), Urfa (37° N.), Mosul (36.5° N.)

*Read before the American Society of Tropical Medicine, New Orleans, May, 1911.

¹RUSSELL, ALEX. The Natural History of Aleppo and Parts Adjacent, London, 1756.

²WILLEMIN, A. Mémoire sur le bouton d'Alep. *Gaz. méd. de Paris*, avril, 1854.

and Bagdad (33.5° N.) in Kurdistan and Mesopotamia. According to Lachéze, the "bouton" was known in Teheran (35.5° N.) and Tabriz (38° N.) in Persia. On the Island of Crete and at Cairo. In Russell's description, three species of sores are mentioned: "male," "female" and a third variety attributed to the bite of a "thousand leg;" the Arab name for the affection being known as "Khars el Umm-Aly" (bite of the mother of Aly), the term Aly referring to *Oniscus murarius*. The numerous contributions to the subject during the last half century can be found in Hirsch,¹ Scheube,² and Marzinowsky.³

GEOGRAPHICAL DISTRIBUTION.

OLD WORLD. At the present time we know that the affection is widely, though not diffusely distributed, in many tropical and sub-tropical countries. Its presence as confirmed by microscopic diagnosis, has been noted in the following places: Europe, Greece (Cardamatis⁴); the Crimea: (Scheube). Transcaucasia, in Lenkoran and Elizabethspol, where it is called "Godowik" and "Il-jarassy" (Marzinowsky). Turkey, in Asia: Syria: Aleppo, where it is known as "Aleppo boil;" "Haleb Choban." Crete: Armenia; Mesopotamia. Asia: Persia, where it is known as "flybite," "annual," "yearly boil." Turkestan, "Pendjeh ulcer." India: The Punjab, Rajputana States and the Northwest Provinces, where it is known as "Delhi Sore." Africa: Egypt, Tunis, in the Sahara of Tunis, where it is known as Gafsa boil ("clou de Gafsa"). Algeria: In the Algerian Sahara, where it is known as the "Sahara chancre"; "Biskra button," "Bouton de Ziban" ("hhabb-el-seneh"), (button of a year, Arabic), "Dous el kourmati" and "Bess el temeur" ("the date disease").

NEW WORLD. The geographical distribution of Oriental sore in the New World is at present apparently limited to certain localities where laboratories for medical research have been established and where special efforts have been made to discover the disease. When research becomes more widely diffused, the disease, no doubt, will disclose a wider distribution.

¹HIRSCH. *Handb. der hist. geogr. Path.* 1886, iii, 467.

²SCHEUBE. *The Diseases of Warm Countries*, P. Blakiston's Son & Co. Philadelphia, 1904.

³MARZINOWSKY. *Zeitschr. f. Hyg. u. Infektionskrankh.*, lviii, 327.

⁴CARDAMATIS, J. P. *Bull. Soc. path. exot.*, Paris, May 12, 1909.

Wright's case of Oriental sore, from which the pathogenic agent was first described, was not an autochthonous one, the patient being an Armenian girl, nine years of age, and having acquired the infection two or three months before she had left Armenia. The first note of its appearance in America is by Moreira¹, who, in 1896, reported its occurrence in Bahia, Brazil. The diagnosis, however, was made by clinical and not by microscopic examination, for the pathogenic agent was not known at that time. Lindenberg, Carini and Paranhos² reported, in 1909, a few cases seen at Baurú, São Paulo, Brazil, among Syrian and Brazilian laborers. A single case has been reported from Guiana.³

In August, 1910, I discovered a case of Oriental sore in a negro who had been living in the bush on a rubber plantation outside of Las Cascadas, C. Z. This discovery of an autochthonous case in the Canal Zone led to a careful search for others, and from among the suspicious cases sent to me recently for diagnosis, I have found three others. With the above, these are the only reported cases of Oriental sore in the New World confirmed by microscopic examination.

CLIMATOLOGICAL FACTORS.

According to Hirsch, Boudin, Laveran, and others, there is a definite seasonal variation to the incidence of infection. At Biskra and in the Caucasus, the boil appears most often in the autumn, September to October. At Biskra, a French garrison of 762 men had 105 men infected, and of these, 30 were infected in November, 59 in December, and 15 in February. In some places, as Aleppo and Bagdad, the disease is seen throughout the year, but the autumnal rainy months are those of its maximum prevalence. It will probably be found that this is related to the prevalence of insect carriers of the disease, flies or mosquitoes, for instance.

It has been noted by writers on the subject that while the disease is rife in certain towns, it may be quite unknown in other places several miles off—that certain places are endemic foci of the disease and remain so—differing in this respect from kala azar, which is caused by a protozoön, resembling very closely that of Oriental sore, which seems to spread over a country like a ringworm, but

¹MOREIRA, JULIANO. *Monatsh. f. prakt. Dermat.*, 1896, xxii, 592.

²LINDENBERG, CARINI and PARANHOS, *Revista Medica de São Paulo*, Brazil, March 31, 1909.

³NATTAN-LARRIER, TOUIN and HECKENROTH. *Bull. Soc. path. exot.*, 1909.

leaving a place comparatively clean after it has passed on. From this peculiar localizing feature of the infection, and on account of our ignorance of other determining factors in the infection, it would be hazardous to say that the disease should certainly be encountered in the Southern States and Mexico, but from a comparative examination of the average temperatures and of the latitude of certain infected places in the Old World with those of some of the cities of the Southern States and Mexico, we have a strong indication from analogy and from the fact that it exists in some places in the New World, that it will be found in the Southern States when especially looked for.

Location	Latitude	For year	AVERAGE TEMPERATURES (Centigrade).			
			For 3 Winter months.	For 3 Spring months.	For 3 Summer months.	For 3 Autumn months.
Aleppo	36.11°N	17.6	6.3	13.4	27.2	18.9
Algiers	36.47°N	17.8	12.4	15.5	23.6	19.9
Tunis	36.48°N	20.3	13.2	18.3	28.3	21.9
Saharanpore	29.57°N	22.4	12.2	24.8	30.0	22.2
New Orleans	29.58°N	21.1	15.1	21.7	28.2	21.4
Savannah	32.5 °N	19.3	11.5	19.6	27.0	19.4
Mexico	19.26°N	16.6	13.0	18.1	19.1	16.2
Nashville	36.10°N	15.0	4.5	15.8	25.2	14.6

Latitudes of the following places where cases of Oriental sores have been detected: Gafsa, 34.5°N., Biskra, 34.5°N., Bagdad, 33.5°N., Elizabethspol, 42.0°N., Crimea, 45.°N., Greece, 34.40°N., Delhi, 28.5°N., São Paulo, 23.5°S., Panama, 9.°N.

It would seem, then, that we might expect to find Oriental sore in America, between, say latitudes 40° S. and 40° N. in localities having an average annual temperature of 17.6°, or more, and in which the average winter temperature is not lower than 6.3°.

PATHOGENIC AGENT.

In the light of our present knowledge, we may dismiss the accounts of pathogenic agents which refer to various parasitic ova, etc., as being of no value—distoma ova (Smith, 1868); parasitic ova (Fleming, 1873) mycelium of a fungus (Carter, 1875); cocci, and other microorganisms.

Cunningham,¹ in 1885, described parasitic microorganisms in a section of tissue from one specimen of a Delhi boil, but his description conforms more closely to those of blastomyces or cell degenerations than to the pathogenic agent, *Leishmania tropica*. The following year Riehl² published his findings in a case of "Orient beule."

¹ CUNNINGHAM, *Sci. Mem. Med. Offic. Army of India*, 1885, i, 21.

² RIEHL, *Vierteljahrsschr. f. Dermat. u. Syph.*, 1886, 805.

Riehl's bodies were described as encapsulated micrococci in large epithelioid cells.

Subsequent to this, micrococci were cultivated from ulcers of this class by a number of workers; but as the protozoal bodies, *Leishmania tropica* are in ulcers frequently associated with micrococci, the presence of the latter must be regarded as that of commensals.

Borowski,¹ in 1898, described bodies obtained from twenty cases of the "Sarten boil." These answer well to the description of *Leishmania tropica*, as do those of Bogorás,² who studied his organism in sections of tissue from the lesion called "Godowik." Schulgin³ confirmed the findings of Bogorás and suggested that the disease might be transmitted by mosquitoes. As well as one can make out from the descriptions in the literature, Borowski was the first to describe from skin ulcers the bodies now known as *Leishmania tropica*. It was Wright,⁴ however, who, from a careful study of the morphology of the parasite in smears and sections of an Armenian boil stained by a modification of Leishman's modification of the Rowmonowsky stain and by his beautiful photomicrographs, placed the matter in a clear light. Subsequent research by Marzinowsky, Bogrow, Plehn and James have established the fact that *Leishmania tropica* is the pathogenic agent of Oriental sore. More recently, very important work has been done by Row, Carter and particularly by Nicolle, at Tunis, on the cultural and immunological characters of the parasite.

In smears from the ulcers, or in films taken from serum expressed from the nodules, small, oval, round or oat-shaped bodies are found in the cytoplasm of large mononuclear cells. They have a large purple staining mass placed at the periphery and a smaller, more deeply staining rod, or dot, the kinetonucleus, always placed a short distance from the trophonucleus and at different angles with respect to it and the long axis of the parasite. The cytoplasm stains faintly blue as in the malarial parasite and there are small acromatic spaces or lines in some of the specimens seen here, exactly like those in the Gregarine phase of *crithidia*. The microorganisms vary somewhat in size in different ulcers but are usually five or six microns in length, 3 to 3½ microns in breadth, the length of the kinetonucleus about 1.5 microns and the diameter of the trophonu-

¹ BOROWSKI. *Milit. Med. Jour.*, 1898, 925.

² BOGORÁS. *Arbeits. d. II Kongr. d. kaukas. Ärzte.*

³ SCHULGIN. *Russk. Vrach.*, 1902, No. 32 u. 33 s. 1150 u. 1180.

⁴ WRIGHT, J. H., *Journ. Med. Res.* 1903, x 472.

cleus about 2 to 2.75 microns. These bodies described by Wright under the name *Helcosoma tropicum* have been cultivated by Row, Carter and Nicolle; on special media they become flagellated and resemble very closely the gut flagellates of insects—*Crithidia* and *Herpetomonas*. Those studied by Nicolle are certainly *Herpetomonas*. These flagellates, as is well known, are closely related to trypanosomes; *Crithidia*, such as are found in biting flies, and fleas, resembling trypanosomes more closely than *Herpetomonas*. I feel very certain that these parasitic intracellular bodies in man—*Leishmania tropica* and *Leishmania Donovanii*, have an extra-corporeal existence in the intestinal tract or biting parts of some representatives of the *Diptera*. The pathogenic agent of Oriental sore is morphologically indistinguishable from the bodies found by Leishman and Donovan in the spleen of patients dying of kala azar, a fatal cachexial disease of Asia, and by Nicolle, in infantile kala azar of the Mediterranean.

As the bodies found in kala azar have been named by Ross, *Leishmania Donovanii*, it has become necessary to call the bodies discovered by Wright *Leishmania tropica*. Some confusion in nomenclature has arisen from the fact that Cunningham, in 1885, described certain bodies in the cells of tissue from a case of Delhi sore, and in confirming his results later, Firth proposed the term *Sporozoa furunculosa*, the specific term of which Blanchard believes should be retained for the parasite of Oriental sore. The question hinges on the identification of Cunningham's bodies with those of Wright. In my opinion it does not seem possible that the bodies described by Cunningham were the ones we now recognize as *Leishmania tropica*.

While the parasites of kala azar and Oriental sore resemble one another very closely; there are certain biological differences; for instance infections by *Leishmania tropica* are confined to the skin, particularly those portions exposed to sunlight, while in infections by *Leishmania Donovanii*, the deeper internal viscera are invaded, suggesting that *Leishmania tropica* requires sunlight and *Leishmania Donovanii* the darkness, and further that *Leishmania tropica*, in its insect host, enjoys the more or less well-lighted translucent medium of a mosquito or fly exposed to daylight, in contrast with *Leishmania Donovanii*, which, from Captain Patton and Rogers' researches, is known to demand the relatively darker medium of the nocturnal daylight-shunning bedbug. Another essential difference between the two microorganisms, as pointed out by Minchin¹ is its

¹ MINCHIN. Letter to British Medical Journal, Aug. 3, 1909.

behavior with sodium citrate, *Leishmania tropica* failing to develop in this medium, while as Rogers discovered, *Leishmania Donovanii* develops a flagellum. Minchin believes that this fact indicates a difference, too, in the mode of transmission of the two parasites.

SUSCEPTIBILITY.

From the time of Russell's account, all writers have noted that the sore attacks all persons without exception, and at Aleppo, most often during the first three years of life. It is rare for an Aleppin to reach the seventh year without being infected.

IMMUNITY.

It is generally recognized that one attack of Oriental sore usually confers immunity against a subsequent one. The Jews of Bagdad were in the habit of inoculating their children on the body with virus from a sore so that they might not later suffer a disfiguring scar on the face.

MODE OF INFECTION.

Russell and Volney attributed the infection to some toxic agent in water, but this theory has now been entirely abandoned. In connection with their theory it should be mentioned that from Patton's researches and those of others, we have become aware of the presence of flagellates in a large number of insects. Patton, for instance, finding them in the water bug *Gerris fossarum*—(*Crithidia gerradis*). Now it may be possible under certain circumstances for various water bugs to cause the infection.

I have pointed out in another place¹ that the location of the lesion often corresponds with the location of the bites of *Stegomyia calopus*. Our cases here, however, have never developed in towns where the *Stegomyia* thrives, but out in the bush where *Tabanids* and other sylvan varieties of flies or mosquitoes prefer to live. It is very likely in certain endemic centres in the East—cities and towns—that *Stegomyia*, or other essentially town-breeding mosquitoes will be found to be the carriers, while in other places, where the disease is most often encountered in the bush, that horse flies and sylvan species of flies or mosquitoes will be incriminated. Until we have more definite knowledge, all invertebrates harboring *Crithidia* or *Herpetomonas* must be held under suspicion. It has long been

¹DARLING. Oriental Sore in Panama. *Arch. Int. Med.*, 1911, vii, p. 581-597.

noticed that the disease became more pronounced as the date season came in, and it was concluded from this that the disease was due to eating unripe dates, but we can see that the date season merely corresponds with the mosquito or fly season, just as here in the Canal Zone the mangoes begin to ripen in numbers with the onset of the rains. Similarly, there is a common belief among some of the natives here that if foreigners eat the mangoes, they will get the "fièvre" (yellow fever). This is merely an expression of the fact that the mosquitoes multiply in numbers after the rains.

In the dissection of suspected insects for flagellates, the salivary glands and sucking parts should be scrutinized as well as the intestinal tract, for the former may be the only means of infecting. On the other hand, of course, it is possible for open cuts to be infected by means of the post-flagellate phase of the flagellate in the fœces of the insect.

INOCULATION EXPERIMENTS.

During the occupation of Egypt by the French, some early attempts at inoculation were made, and it is said that "buttons" of short duration were produced. Willemin inoculated a number of children and some adults, and in a few instances succeeded in producing a sore. Willemin also mentions the fact that he saw two dogs with "buttons" on the extremities of their muzzles. It should be mentioned that Nicolle has recently succeeded in infecting dogs on the muzzle with the Biskra button.

Nicolle's¹ researches on Oriental sore carried out at Tunis are most complete. He and Manceaux have identified the "Clou de Gafsa" with other varieties of Oriental sore, and they found that the pathogenic agent, *Leishmania tropica*, had the same morphological characters and the lesions were identical. Cultures of *Leishmania tropica* were obtained easily, using blood agar. The cultures developed and lived for several weeks at a temperature of 22°C. When cultures from man were inoculated into either man or monkeys, typical "boutons" were produced, even with the fourth generation of cultures, the period of incubation being 16 to 166 days. Constant and positive cultural results with the experimental virus could only be obtained with material from the very young "boutons." The virus of Oriental sore is inactive for the goat, cat, sheep, wild rat, horse and ass. Curiously, the region of election for successful in-

¹ NICOLLE et MANCEAUX. Recherches sur le bouton d' Orient cultures, reproduction expérimentale, immunization. *Ann. de l'Institut Pasteur*, xxiv, 673.

oculation in the monkey and dog is the nose. Subcutaneous inoculation on the body was negative. The inoculation of 100 cultures of *Leishmania tropica* into the peritoneal cavity of a dog did not confer any immunity upon subsequent inoculation into the skin. They state that there is reason to suspect the dog as being a natural reservoir for the virus of Oriental sore and that this animal plays a capital rôle in the ætiology of Leishmaniosis. Possibly the raccoon is equally susceptible, for I have found that the dog and the raccoon react in an almost identical manner with a trypanosome (*Trypanosoma hippicum*).

THE SORE: APPEARANCE, LOCATIONS, TYPES.

The sore appears first as one or more papules, usually on some exposed part of the body, as the ear, face, forearms or legs. The other parts of the body are much less susceptible to primary infection, but they are susceptible to autoinoculation. Several types of lesions are seen: The non-ulcerative or nodular type is one. This may be single or multiple. There are also abortive nodules which develop no further than the papular stage and then disappear without ulceration. A common type is a solitary ulcer. Multiple ulcers and a spreading ulcerative form, common in autoinoculations, are seen. The sore may develop from what is apparently an insect bite, a very definite fly bite, or by the infection of any break in the skin. Nicolle determined, experimentally, that the period of incubation was 16 to 166 days. In the typical ulcer there are four stages: (1) infiltration, proliferation and induration; (2) desquamation; (3) ulceration or involution; (4) cicatrization. The chief character of the ulcerative process is an erosive one and its tendency to become a little larger as each scab is renewed until the maximum size is attained. The papule may from the first discharge turbid serum, which coagulates into a tough scab. There is considerable itching during the papular stage and some writers mention that fever and malaise are present in some cases. The ulcer may reach the size of 6 or 8 cm. in diameter and after existing for from several months to a year, or a year and a half, the scab becomes progressively smaller and cicatrization occurs, leaving a permanent scar.

DIAGNOSIS.

Considering the protean character of the lesion, a positive diagnosis can only be made by finding the pathogenic agents in smears or sections of tissue. They are seen in greater abundance in the

younger lesions, but may be found in all, if sufficient pains are taken in the search for them. When sparse I have found them in somewhat larger numbers at the periphery of the ulcer than toward the centre.

Film preparations of the microörganism from different cases contain bodies differing slightly from one another, though approaching the type very closely. Sometimes the bodies are all quite globular; in others, more attenuated or oat-shaped. Their size varies, too, indicating that different species of flagellates may be concerned in the infection. In the older ulcers, when the bodies are sparse, it is not uncommon to find a few extracellular, degenerated oval or oat-shaped bodies devoid of chromatin. When these are encountered, a careful search will usually reveal typical bodies.

The lesions at different stages and of different types have to be differentiated from the following conditions, but this can be done with certainty only by finding the pathogenic agent: Furunculosis, rodent ulcer, lupus, keloid, infected mosquito and tick bites and ulcers, ecthyma, impetigo, extra-genital chancre, dermatomycoses, tropical ulcer and yaws. On account of this resemblance to other infections, James¹ remarks will bear repeating. "The appearance of some true Oriental or Delhi sores is by no means so characteristic as one would expect it to be from the descriptions in books and I found that the Civil Surgeons, whose experience with the disease was considerable, were often unwilling to express a definite opinion as to whether a given sore was really an Oriental sore, or whether it was an example of the ordinary chronic ulcer so common among natives of India. When I say that the first example of an Oriental sore seen by me in Delhi appeared at a superficial examination to be more like a ringworm than anything else, and that I at first considered another Oriental sore to be an ordinary "shoe bite" it will be apparent that I have felt a similar difficulty in diagnosis."

In these words James expresses the difficulty of diagnosis and shows that Oriental sore does not always present very distinctive characters, and here is to be found the explanation of the failure of a number of competent observers to find *Leishmania tropica* in certain types of tropical ulcers.

HISTOPATHOLOGY.

The accounts of the histology of the sore vary somewhat, but may be explained on the ground that such descriptions have been

¹ JAMES. Oriental or Delhi Sore. *Sci. Mem. Off. Med. San. Depart. Govt. of India*, N., series 13, 1905.

based on sores of different ages and those evoked by microorganisms, possibly of different species and of different degrees of virulence. Early, there is atrophy of epithelium and disappearance of the papillæ, with a proliferation of round and endothelial cells, the latter containing the pathogenic agent. Later, there is metaplasia of the epithelium and sometimes a few giant cells are seen. There are many epithelioid cells and fewer parasitized endothelial cells. The sweat glands and the perivascular lymph spaces show considerable invasion by round cells. Coincident with ulceration, there is a secondary invasion by skin cocci and a slight leucocytic exudation.

TREATMENT AND PROPHYLAXIS.

Until the exact mode of infection has been ascertained it will be impossible to adequately protect against the infection.

The ulcers should be kept surgically clean and protected from flies, etc., by dressings. The addition of some member of the coal-tar group, distasteful to flies, such as "creolin" or "kreso" is recommended.

All writers on the subject are agreed that external applications are not always effective in removing the sore. Early, free excision should be practiced whenever possible. Marzinowski has successfully treated a number of cases by freezing the "button" with ether. Castellani advocates the use of protargol. Among other substances used are tincture of iodine, 10 per cent.; methylene blue, 10 per cent.; powdered permanganate of potash; ferropyrin; bromide of quinine, etc. Duncan advises the application of a thin piece of lead over the ulcer, the rationale of which is rather obscure, unless it be that the lead prevents the access of sunlight. In view of the suspicion that *Leishmania tropica* requires sunlit subcutaneous tissue to develop in, this method of Duncan's deserves further trial.



